

Background: The HCT-CI is a comorbidity score adapted to hematopoietic cell transplantation, which has identified 3 risk groups with increased non-relapse mortality (NRM) and lower overall survival (OS) (Blood 2005;106:2912). We determined the HCT-CI score in a cohort of patients who underwent myeloablative MUD transplantation in a single institution trial. **Methods:** The analysis included all patients undergoing MUD transplant from 1996–2006 who received a 3-drug GVHD prophylaxis regimen. Comorbidities were obtained by retrospective chart review and scored according to the HCT-CI score. **Results:** 150 patients (median age 40) were included, with 38% low-, 34% intermediate- and 28% high-risk disease, per CIBMTR classification. Diagnoses included acute leukemia in 50%, MDS in 12%, CML in 15%, and lymphoma in 18%. Conditioning regimens were Cy-TBI in 64% and Bu-Cy in 21%. HCT-CI scores of 0, 1–2 or ≥ 3 were found in 17%, 30% and 53% of patients. The majority of comorbidities were pulmonary (72%). Day 100 and 5-year OS were 82.7 and 33%, with a 23% and 50.4% cumulative incidence of NRM. Five year relapse-related mortality was 15.8%. No statistically significant differences in NRM or OS were detected using the HCT-CI grouping of 0, 1–2 and ≥ 3 . Unadjusted hazard ratio (HR) for inferior survival were 0.9 (CI 0.47–1.85, $P = .79$) and 1.65 (CI 0.885–3.090, $P = .11$) for scores 1–2 and ≥ 3 , respectively. We determined an alternate prognostic model based on 2 groups. Statistical modeling separated patients with a score of 0–3 ($n = 97$, 64%) and ≥ 4 ($n = 53$, 35.6%), with a 3 month and 5 year OS of 84% and 45% versus 52% and 10%, respectively ($P < .0001$). Cumulative incidence of day 100 and 5-year NRM was 16% and 38% versus 43% and 73%, respectively. Unadjusted HR for inferior survival was 2.77 (CI 1.816–4.225, $P < .0001$) for a score of ≥ 4 . By multivariate analysis, only the HCT-CI score ($P < .0001$) and the disease risk per CIBMTR ($P = .0058$) were predictive of OS and NRM, but not age, CMV status, sex- or HLA-mismatch, or regimen. **Conclusions:** Although the HCT-CI score was predictive of NRM and OS in this high-risk cohort, we were unable to detect statistically significant differences between the 3 risk groups defined in the original score. A modified 2-group scoring system of 0–3 and ≥ 4 , respectively, identified a low-risk and a high-risk group. This simplified, 2-tiered scoring system will have utility in clinical decision-making and in defining patients eligible for clinical trials.

286

LIPOPOLYSACCHARIDE BINDING PROTEIN PROMOTER VARIANTS INFLUENCE THE RISK FOR GRAM-NEGATIVE BACTEREMIA AND MORTALITY AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

Chien, J.W., Boeckh, M., Hansen, J.A., Clark, J.G. Fred Hutchinson Cancer Research Center, Seattle, WA.

Lipopolysaccharide binding protein (LBP) function is dependent upon circulating LBP levels. Disturbance of LBP transcription regulation may influence the risk for clinical events. We comprehensively assessed the LBP sequence and identified three haplotype tagging single nucleotide polymorphisms (SNPs) for our studies. Using a nested case control design, we assessed whether genetic variation in the LBP gene influences the risk for Gram-negative (GN) bacteremia after allogeneic hematopoietic cell transplantation (HCT), then confirmed the associations by prospectively assessing association with an intermediate phenotype (circulating LBP levels) and a secondary clinical phenotype (mortality). Presence of the SNP 6878 C allele among patients was associated with a two-fold higher risk for GN bacteremia (odds ratio 2.22, $p = 0.001$). SNP 6878 was in strong linkage disequilibrium with three SNPs in the LBP promoter, one of which was SNP 6878 ($r^2 = 0.8$), located in a promoter CAAT box. The SNP 1683 C allele was associated with higher median circulating LBP levels (TT 10.86 \pm 0.68 mg/ml; TC 13.86 \pm 1.51 mg/ml; CC 20.66 \pm 5.89 mg/ml; $p = 0.002$) and a three-fold increase in mortality risk (hazard ratio 3.30, $p = 0.001$). These data suggest that genetic variation in the LBP promoter variation likely influences the risk for developing GN bacteremia and death after HCT.

287

HEMATOPOIETIC CELL TRANSPLANTATION (HCT) FOR CHEMORADIO-THERAPY-RELATED MYELODYSPLASTIC SYNDROME AND ACUTE LEUKEMIA: A SINGLE-CENTER ANALYSIS OF 47 PATIENTS

Yokoyama, H., Fukuda, T., Kobayashi, Y., Kim, S.-W., Maruyama, D., Mori, S.-I., Watanabe, T., Tanosaki, R., Tajima, K., Tobinai, K., Takaue, Y. National Cancer Center Hospital, Tokyo, Japan.

Purpose: To examine the value of allogeneic HCT in the treatment of therapy-related myelodysplastic syndrome/acute leukemia (t-MDS/t-AL) which develops after previous exposure to chemotherapy (CT) or radiotherapy. **Patients and Methods:** We retrospectively analyzed the data of 47 patients who were treated at our institution between 1996 and 2007. The primary diseases included malignant lymphoma ($n = 17$), breast cancer ($n = 13$) and other solid tumors ($n = 17$). The median interval between the diagnosis of the primary disease and the onset of t-MDS/t-AL was 3.9 years (range, 0.6–18.7). Twenty-five patients had AML, 5 ALL, 1 biphenotypic acute leukemia, and 16 MDS. **Results:** Thirty-three patients received disease-adapted CT, with a response rate of 73%, while 14 patients were elected to receive no interventions due to an indolent clinical course such as MDS-RA ($n = 13$). With a median follow-up of surviving patients of 1.9 years (range, 0.05–10.5) after the diagnosis of t-MDS/t-AL, the 3-year OS for all patients was 55%. Twenty-seven patients (median age, 47 years; range, 3–63) underwent allogeneic HCT from related ($n = 12$) or unrelated ($n = 15$) donors after myeloablative ($n = 18$) or reduced-intensity ($n = 9$) conditioning regimens. The sources of stem cells were BM in 15 patients, PBSC in 10, and CB in 2. At the time of HCT, 18 t-MDS/t-AL were in CR, 1 was in non-CR, and 8 had untreated t-MDS. Twenty patients (43%) did not undergo HCT due to various reasons, including age older than 65 years ($n = 11$), indolent clinical course ($n = 4$), progression of the primary disease ($n = 4$) or t-AL ($n = 3$), and patient refusal ($n = 2$). The 3-year OS was significantly better in patients who received HCT than in those who did not (71% vs 31%; $P = 0.018$). TRM after HCT was 15%. The 3-year OS was better in those who achieved CR after initial therapy for t-MDS/t-AL than in those who did not (74% vs 30%; $P = 0.002$). A multivariate analysis revealed that HCT was associated with a significantly better OS, even after adjusting for age and other significant prognostic factors including achievement of CR in t-MDS/t-AL, cytogenetic risk group, and an interval between the diagnosis of primary disease and t-MDS/t-AL of longer than 3 years. **Conclusion:** Although this study is contaminated by a selection bias, it still appears that HCT was an effective therapeutic option for patients with t-MDS/t-AL, especially when patients were in CR. These results support a prospective study to examine the value of upfront HCT.

288

HEALTHY ALLOGENEIC RELATED DONORS OF PERIPHERAL HAEMATOPOIETIC PROGENITORS: A LONG-TERM PROSPECTIVE STUDY

Tassi, C.¹, Arpinati, M.², Giudice, V.¹, Bontadini, A.¹. ¹ Sant'Orsola-Malpighi Policlinic, Bologna, Italy; ² Sant'Orsola-Malpighi Policlinic, Bologna, Italy.

One hundred and thirty six healthy donors who underwent apheresis collections after G-CSF stimulation have been included in a surveillance protocol for a provisional period of ten years. Once a year, they are required to send a WBC, Hb and platelets count report and clinical information to our Service. To date, the mean observation time is 46(4–120) months. Fifty out of the 136 donors show a follow-up longer than 60 months. As previously described (1), at day +14 after G-CSF administration, a moderate neutropenia or lymphocytopenia, have been documented in 32 and 20 subjects, respectively. Moreover, a mild thrombocytopenia has been diagnosed during the G-CSF administration in 52 donors. After a five years period of observation, a persistent, slight reduction of circulating neutrophils or lymphocytes has been detectable in 5/32 or 5/20 donors, without clinical relevance. As regards clinical data, 1 case of MGUS, Insipid Diabetes, Autoimmune Thyroiditis, Multiple Sclerosis, Intestinal Multiple Polyps and Allergy to certain food, were the main diseases reported by six donors. Four donors